REMARKS

The present application was filed on April 24, 2001 (claiming priority from United States Provisional Application Number 60/237,590, filed October 3, 2000) with claims 1-28. Claims 4-16, 20-22 and 26-28 have been withdrawn from consideration in response to a restriction requirement. Claims 1-3, 17-19 and 23-25 are therefore currently pending in the application.

In the outstanding Office Action, the Examiner objected to the specification based on embedded hyperlinks and/or browser-executable code appearing therein. The Examiner rejected claims 1-3 under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. Specifically, the Examiner stated that the instant claims do not specify how the results of the method are either concrete, tangible or useful. The Examiner further rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §101 as allegedly lacking patentable utility. Specifically, the Examiner asserted that the specification lacks teaching of any utility for the claimed method wherein expression signal data is transformed.

The Examiner rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Namely, the Examiner asserted that the phrase "transformation that renders," appearing in claims 1, 17 and 23, is unclear. The Examiner also asserted that the limitation of rendering uniform a probability distribution, as in claims 3, 19 and 25, is unclear. The Examiner further asserted that the term "mapped," as recited in claims 3, 19 and 25, is unclear.

The Examiner rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §103(a) as allegedly unpatentable over Eisen, et al. *Cluster Analysis and Display of Genome-Wide Expression Patterns*, PROC. NATL. ACAD. SCI., vol. 95, pp. 14863-68 (December 1998) (hereinafter "Eisen").

The present invention relates generally to the characterization of phenotypes by gene expression patterns. In one exemplary aspect, a plurality of gene expression signals are

determined for a gene. A transformation is derived that renders uniform, within a selected interval, a distribution of transformed gene expression signals for the gene.

FORMAL REJECTIONS

In the Office Action, the Examiner objected to the specification based on embedded hyperlinks and/or browser-executable code appearing therein. Namely, the Examiner objected to the hyperlink appearing on page 26 of the specification. To address the Examiner's objections, Applicants have deleted all hyperlinks appearing in the application, e.g., those appearing on pages 15 and 26 of the specification.

As mentioned above, the Examiner rejected claims 1-3 under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. The Examiner submitted that the present method does not meet the standards of being immediately useful as "there is no specificity identified as to what is intended by the outcome of the method." Further, the Examiner stated that "there is no recitation of what to do with the ... [result of the method] or how ... [the] result of the method is concrete, tangible or useful." See Office Action, page 3, 1st paragraph. Applicants respectfully disagree with the Examiner's assertions.

Claim 1, from which claims 2 and 3 depend, recites deriving a transformation. The transformation renders uniform, within a selected interval, a distribution of transformed gene expression signals. The Examiner's assertion that the derived transformation, a result of the method, is not a concrete, tangible or useful result is contrary to the overall teachings of the application. By way of example only, a derived transformation may be described as a non-linear similarity metric that maximizes the probability of discovering discriminative gene expression patterns. See, specification, page 14, lines 15-17. Therefore, the transformation of the input expression signals, a concrete and tangible result of the instant techniques, is useful, for example, in discovering gene expression patterns.

The Examiner also rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §101 as allegedly lacking patentable utility. Specifically, the Examiner asserted that while the specification teaches that transformations of data can be used for the identification of phenotype patterns, the claimed method is only directed to transforming data that represents gene

expression signals. According to the Examiner, the specification does not teach any specific, substantial, or well-established utility for a method that simply transforms expression signal data.

This is not the case. The specification clearly teaches that transformations are derived, wherein a probability density distribution is transformed into a uniform probability density. See, for example, page 14, lines 9-12 of the specification; FIG. 2. The transformations can then be applied to a phenotype matrix. See, for example, page 14, lines 24-25 of the specification. Therefore, the transformation has both specific and substantial "real world" utility according to the guidelines provided in M.P.E.P. §2107.01.

Further, as understood, the argument presented by the Examiner does not make any sense. As the Examiner in fact highlights, the transformation can be "used" (i.e., has utility) in identifying phenotype patterns. Thus, a conclusion that techniques directed to deriving a transformation that renders uniform a distribution lack utility is baseless.

The Examiner rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner rejected claims 1, 3, 17, 19, 23 and 25 based on the phrase "transformation that renders uniform," appearing in claims 1, 17 and 23 and the phrase "transformation renders uniform a probability distribution," appearing in claims 3, 19 and 25. The Examiner questions how uniformity of a distribution is defined.

Applicants respectfully submit that the limitation of rendering uniform a distribution, e.g., a probability distribution, as recited in claims 1, 3, 17, 19, 23 and 25, is clearly presented in the specification in a way that would allow one of ordinary skill in the art to assess the scope of that limitation. By way of example only, the specification teaches that the probability distribution of a gene, e.g., the probability that the gene expressed itself at a particular value (for example, based on the amount of luminescence detected from points on a gene microarray), may be converted to a uniform distribution (using a transformation) by performing an integral of the probability density function. See, for example, page 8, line 25 through page 9, line 6. That teaching combined with the basic concept of a uniform distribution, which would be apparent to one having ordinary skill in the art, illustrates that the instant specification clearly sets forth the metes and bounds of the present claims.

The Examiner also rejected claims 3, 19 and 25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner rejected claims 3, 19 and 25 based on the phrase "wherein each gene expression signal is mapped by the transformation into a transformed gene expression signal." The Examiner questions what is meant by the term "mapped" and whether the signal is physically mapped somewhere.

Applicants point out that the term "mapped" is a common term of art indicating a correspondence, not a "map" as the Examiner suggests. By way of example only, the Merriam-Webster's Collegiate Dictionary, tenth edition, defines the term "mapped" as to assign (as a set or element) in a mathematical correspondence.

PRIOR ART REJECTIONS

As mentioned above, the Examiner rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §103(a) as allegedly unpatentable over Eisen. Applicants respectfully disagree with the Examiner's rejections.

Eisen is directed to the analysis of gene expression patterns using hierarchical clustering methods combined with colored graphical representations of the data. For example, genes are represented by a tree structure whose branch lengths reflect similarities, as well as more distant relationships, among groups of closely related genes. See Eisen, page 14863.

Applicants cannot find any teaching in Eisen of deriving a transformation that renders uniform a distribution of transformed gene expression signals, a limitation present in each of Applicants independent claims 1, 17 and 23. Applicants respectfully submit that such a teaching is not present in Eisen, and Eisen is merely directed to clustering techniques. As highlighted by the Examiner, Eisen at page 14867, states that clustering algorithms are used and alternative clustering techniques, such as parametric ordering and supervised clustering, are being explored. As such, Applicants respectfully submit that the present claims are non-obvious over the teachings of Eisen.

In view of the foregoing, the invention, as claimed in claims 1-3, 17-19 and 23-25, cannot be said to be suggested by Eisen. Accordingly, Applicants submit that all of the

pending claims, i.e., claims 1-3, 17-19 and 23-25, are in condition for allowance and such favorable action is earnestly solicited.

If any outstanding issues remain, or if the Examiner has any further suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

The Examiner's attention to this matter is appreciated.

Respectfully submitted,

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